Applicant: James Keck et. al Attorney Docket No.: 0119368-00021/2307US Amendment

Serial No.: 09/601,997

Filed : December 15, 2000

## IN THE CLAIMS:

Please amend claims as follows: This listing of claims replaces all prior such listings of claims.

## **LISTING OF CLAIMS:**

Claims 1-8 (Cancelled)

- 9. (Currently amended) The method according to Claim of claim 58, wherein said function is a physiological function.
- (Currently amended) The method according to Claim of claim 58, wherein 10. said function is enzyme activity.
- (Currently amended) The method according to Claim of claim 58, wherein 11. said function is protein synthesis.
- (Currently amended) The method according to Claim of claim 58, wherein 12. said function is expression of a biological factor.
- 13. (Currently amended) The method according to Claim of claim 58, wherein said function is a regulatory effector function.
- (Currently amended) The method according to Claim of claim 58, wherein 14. said phenotypic change is monitored directly.

Claims 15-57 (Cancelled)

- (Currently Amended) A high-throughput method of assigning a function 58. associated with a product coded for encoded by a sample nucleic acid sequence in a target nucleic acid molecule, said method comprising:
- a) without any intervening bacterial cloning steps and without any conformational modeling of mRNA transcribed from the target nucleic acid molecule that comprises the sample nucleic acid sequence in the target nucleic acid molecule, delivering into, and amplifying and expressing a plurality of members of an oligonucleotide family as individual transcription products in a plurality of recombinant non-bacterial host cells comprising the target nucleic acid molecule that comprises the sample nucleic acid sequence, whereby the method is high-throughput, wherein:

each member of the oligonucleotide family comprises a plurality of nucleic acid molecules;

each member of the oligonucleotide family encodes a transcription product comprising a sequence that is complementary to a sequence contained in the mRNA Applicant: James Keck et. al Attorney Docket No.: 0119368-00021/2307US
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transcribed from the <del>target nucleic acid molecule that comprises the</del> sample nucleic acid

transcribed from the target nucleic acid molecule that comprises the sample nucleic acid sequence in the target nucleic acid molecule;

the plurality of members of the oligonucleotide family are introduced into expression vectors, which are introduced into the host cells, wherein the expression vectors comprise:

double-stranded DNA, comprising:

a sense strand and an antisense strand, wherein the sense strand encodes RNA a transcription product that is complementary to and binds to an mRNA sequence transcribed from the sample nucleic acid sequence in the target nucleic sequence molecule so that expression of a product from the target coded for by the sample nucleic acid sequence is inhibited; and

means for determining directionality of expression, wherein the product <u>coded</u> for by the <u>sample nucleic acid sequence</u> is associated with at least one phenotypic property of a host cell containing the mRNA sequence; and wherein the expression vector is for expression in non-bacterial host cells;

the coding sequence for each individual transcription product encodes an antisense nucleic acid that binds to the mRNA transcribed from the <u>sample nucleic acid sequence in the</u> target nucleic acid molecule that comprises the sample nucleic acid sequence; and

expression of one or more of the individual transcription products inhibits production of a product of the mRNA; and

- b) in the resulting host cells, comparing the phenotypes of the resulting host cells to phenotypes of control cells to identify changes in phenotype to thereby assign a function associated with the product encoded by the sample nucleic acid sequence in the target nucleic acid molecule, wherein control cells are untransfected host cells, whereby changes in phenotype can be assigned by comparison of the transfected host eeil cell, and the untransfected host cell.
- 59. (Currently Amended) The method of claim 58, wherein the RNA that is produced transcription product is encoded by from the sense strand of and binds to an mRNA sequence transcribed from the sample nucleic acid sequence in the target nucleic acid molecule sequence so that expression of a product encoded by from the target sample nucleic acid sequence is inhibited, comprises:

transcribed from the sample nucleic acid in the target-nucleic sequence

a catalytic domain that cleaves the mRNA sequence transcribed from the sample nucleic acid in the target nucleic sequence molecule; and Applicant: James Keck et. al Attorney Docket No.: 0119368-00021/2307US Serial No.: 09/601,997 Amendment

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binding sequences flanking the catalytic domain for binding the RNA transcription product to the mRNA, and/or wherein the means for determining directionality of expression comprises a different non blunt-ended restriction enzyme site at each end of said double-stranded DNA.

60. (Original) The method of claim 59, wherein the double-stranded DNA is formed by contacting a first oligonucleotide with a complementary second oligonucleotide, and/or wherein the non blunt-ended restriction enzyme site is complementary to an end of the expression vector.

- 61. (Original) The method of claim 59, wherein said expression vector is formed by: (a) contacting a double-stranded oligonucleotide with an expression vector; or (b) by contacting a single-stranded oligonucleotide with said expression vector; or (c) contacting a triple-stranded oligonucleotide with an expression vector.
- 62. (Previously Presented) The method of claim 58, wherein the expression vector is a plasmid or a virus for expression in non-bacterial host cells.
- 63. (Original) The method of claim 62, wherein the virus is a retrovirus or an adeno-associated virus.
- 64. (Previously Presented) The method of claim 58, wherein the expression vector is transfected directly into mammalian cells.
- 65. (Previously Presented) The method of claim 58, wherein the sample nucleic acid is genomic DNA, cDNA, an expressed sequence tag (EST) or RNA.
- 66. (Previously Presented) The method of claim 58, wherein the family contains between 3 and 20 members.
- 67. (Currently amended) The method of claim 58, wherein each member of the family is designed to inhibit the production of a product of <u>a sample nucleic acid sequence in</u> the target nucleic acid molecule.
- 68. (Previously Presented) The method of claim 58, whereby all members of a family are assessed in a single experiment.
- 69. (Currently amended) The method of claim 58, whereby a plurality of different target nucleic acid molecules and/or comprising sample nucleic acid sequences are assessed.
- 70. (Original) The method of claim 59, wherein the expression vector is a plasmid or a virus for expression in non-bacterial host cells.

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71. (Original) The method of claim 60, wherein the expression vector is a plasmid or a virus for expression in non-bacterial host cells.

- (Original) The method of claim 61, wherein the expression vector is a plasmid 72. or a virus for expression in non-bacterial host cells.
- (Previously Presented) The method of claim 58, wherein the oligonucleotide 73. family is a ribozyme family.
  - 74. (Cancelled)